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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/765,287	09/12/1997	CAMILLE LOCHT	960-25	5876

7590 08/13/2002

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EXAMINER
SHAHNAN SHAH, KHATOL S

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/13/2002 30

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/765,287	LOCHT ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-22,27-30 and 34-41* is/are pending in the application.

4a) Of the above claim(s) *36 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18-22,27-30,34,35, 37 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgement is made of Applicants' response filed 4/18/2002 paper number 29.

2. Claims 1-15, 18-22, 27-30 and 34-41 are pending. Claims 36 and 38 were withdrawn from consideration as being drawn to non-elected inventions.

3. Claims 1-15, 18-22, 27-30, 34, 35, 37 and 39-41 are under consideration.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 or form PTO-1449 have submitted with this office action.

Rejection (s) Maintained

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-15, 18-22, 27- 30 and 39 under 35 U.S.C. 103 (a) as obvious over Loosmore et al. (EP 453216) in view of Menozzi et al. (FEMS Microbiology Letters, 78:59-64, 1991) is maintained for the reasons set forth in the office action mailed 12/18/2001 (paper number 27).

Applicants argue that there is nothing in Loosmore et al. that describes or suggests the construction of a recombinant DNA encoding a fusion protein comprising an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha.

Applicants further argue that Menozzi et al. does not remedy the deficiencies of the primary reference.

Applicants' arguments have been carefully considered, but they are not persuasive. The Examiner respectfully draws applicants' attention to columns 3 and 4 of Loosmore et al. specifically column 4, lines 20- 58, which teach a fusion protein comprising an amino acid sequence from Fha fused to an amino acid sequence from a protein distinct from Fha. Loosmore et al. teach Fhap/TOX, Fhap/PRN and TOXp/Fha, as well as a recombinant strain with kinetics and yields comparable to the wild type strains.

Applicants further argue that Loosmore et al. gene fusions do not code in any way for "fusion proteins comprising an amino acid sequence distinct from Fha". Applicants contend that Loosemore et al. is different from the claimed invention in that the fusion in Loosemore's disclosure is only made between a promoter and a coding sequence.

It is the examiner's position that Loosemore et al. recite in column 2, lines 14-18 " Accordingly, in one aspect, the present invention provides a hybrid pertussis gene, comprising a structural pertussis gene fused at an ATG start codon to be a native but autologous pertussis promoter". Column 2, lines 24-28 further recite, " The present invention further provides a strain of *Bordetella*, particularly *Bordetella pertussis*, which has been transformed by the hybrid gene and is capable of expression of a gene product of the structural pertussis gene". Contrary to applicants' arguments, the hybrid gene generated by Loosemore et al. qualifies as the fusion agent and the gene product expressed by Loosemore's pertussis structural gene qualifies as a " polypeptide heterologous with respect to Fha of *Bordetella*.

With regard to the reference of Menozzi et al. applicants acknowledge that the reference teaches the Fha-heparin interactions, but contend that it does not teach a fusion protein construct comprising a Fha moiety. The applicants ' argument has been carefully considered, but it is not persuasive. The reference of Menozzi et al. has been applied to indicate the art- known fact that the Fha, for example of Loosemore et al., contains the heparin interaction site. The hybrid gene of Loosemore et al. expresses Fha that contains the heparin interaction site and is implicit in the disclosure of Loosemore et al. in light of what is well known in the art, as taught by Menozzi et al. Therefore the rejection based on the above references is proper under 35 U.S.C. 103 (a).

7. The rejection of claims 34, 35 and 37 under 35 U.S.C. 103 (a) over Loosmore et al. (EP 453216) in view of Menozzi et al. (FEMS Microbiology Letters, 78:59-64, 1991) and Locht et al. is maintained for reasons set forth in paragraph 11, page 5 of the office action mailed 9/26/2000 (paper no. 21).

Applicants' arguments have been fully considered, but are not persuasive.

Applicants' arguments concerning Loosmore et al. and Menozzi et al. have been addressed above (see paragraph 6 above).

Applicants further argue that there is nothing in Locht et al. that would have suggested making fusion protein with Fha moiety.

It is the examiner's position that applicants argue the references individually. The rejection was based on a 103 rejection using combination of three references. It is the combination of the references that render the claims obvious. The reference of Locht et al. teaches the immunogenicity of Fha when presented to the mucosal immune system. Given this disclosure, it

would have been obvious to one of ordinary skill in the art at time the invention was made to present Loosmore's composition as modified by Menozzi et al. to the mucosal immune system to produce the instant invention, as set forth on page 7 of the action in paper number19, one of ordinary skill in the art would have been motivated to produce the instant invention in order to achieve effective and long lasting local or mucosal immunity as taught by Locht et al.

8. The rejection of claims 40-41 under 35 U.S.C. 102(e) as anticipated by by Relman et al. is maintained.

The rejection was stated as below:

Claims 40-41 are drawn to the host cells belonging to a bacterial species other than *Bordetella.*

Relman et al. disclose host organisms or strains from pathogens other than *Bordetella.* They disclose other organisms such as *E. coli, Salmonella, Yersinia* or *Pseudomonas* (see column 4, lines 44-48) expressing a fusion protein or hybrid protein comprising a part of the filamentous haemagglutinin or Fha and a part of a protein heterologous to Fha. They disclose seven portions of the Fha B open reading frame were each cloned into the expression vector (see column 9).

Relman et al. disclose that nucleic acid and protein compositions are provided from *B. pertusis*, which may find use in diagnosis and treatment of disease. Particularly they disclose that an open reading frame encoding filamentous hemagglutinin precursors provided, with the intact protein for the filamentous hemagglutinin portion thereof can be expressed in a wide variety of

hosts including *E. coli*, for use in the production of antibodies, for immunodiagnosis or therapy, or as vaccine for prophylactic purposes. (see abstract and claims).

Applicants' arguments have been fully considered, but are not persuasive. Applicants argue " The examiner refers to column 9 of Relman et al. which discloses Fha B fusion proteins. Applicants refer to the same column, especially lines 45-59. This paragraph indeed discloses fusion proteins between part of the Fha and the phage MS2 RNA polymerase. However contrary to the fusion recited in claim 40, these fusion proteins have an N-terminal moiety constituted by the " first 98 amino acids of the phage MS2 RNA polymerase" and a C-terminal moiety consisting of Fha C-terminal fragment". Applicants further argue that "the fusion protein disclosed by Relman et al. have been made to confirm the absence of a transnational STOP codon in various regions of the ORF, it can be understood that the Fha moiety is C-terminal.

It is the examiner's position that Relman et al. do not only teach a C-terminal Fha moiety but also teach a N-terminal moiety consisting of Fha N-terminal fragment (see column 2, lines 30-35, and claims 8-10).

Conclusion

9. Claims 1-15,18-22, 27-30, 34, 35, 37 and 39-41 stand rejected.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

August 8, 2002

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600